ETS AND CANCER OF SITES OTHER THAN THE LUNG

Introduction

A presenter at the recent McGill Symposium in Montreal, Canada, described the then-available epidemiologic studies on ETS and cancer other than the lung as follows:

> These nine studies provide insufficient data to evaluate the effect of ETS on cancer other than of the lung. The reported associations are weak and inconsistent, and are subject to the potential effects of biases and uncontrolled confounding factors . . .[1]

These studies concern a variety of cancer sites; the publications on each are briefly summarized below. Highlighted copies of the papers on cancer at other sites are found at Tabs 1-11.

All Cancers Combined

- Several studies have presented risk estimates for overall cancer incidence, regardless of site, among individuals reporting ETS exposure. This procedure disregards differences in etiology, mechanism and confounding factors among the various types of cancer; nevertheless, some authors have presented data in this fashion.

Hirayama (1984) reported a significant elevation in risk for "cancer of all sites," in nonsmoking women whose husbands

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smoked; he attributed the elevation to increased risks for lung, nasal sinus, and brain cancers.[2]

Miller (1984) reports on a "case-control" study conducted in Pennsylvania by interviewing the surviving relatives of women whose death notices were published in a local newspaper.[3] Miller reported an overall odds ratio of 1.40 for "death due to cancer" among women whose husbands smoked. Questions can be asked about the accuracy of the amount of recall required of the relatives in this study.

In an abstract, Reynolds, et al., (1987) reported that a record-linkage study in Alameda County, CA concluded that nonsmoking women married to smokers had a 70% higher risk of cancer incidence at all sites, and that they had an approximate relative risk of 7.0 for "smoking-related cancers."[4] The abstract provides insufficient information to judge the quality of the study; the reported risk estimates should be viewed with caution.

Sandler, et al., (1989) reported statistically nonsignificant point estimates of 1.01 (males) and 1.00 (females) for all cancers in persons reporting ETS exposure.[5] The authors' subdivision of the category into "smoking-related" and "other" cancers yielded no statistically significant risk estimates. This study was criticized by Holcomb (1989) as being "poor science" and

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"inadequately designed."[6]

Brain and Nasal Sinus Cancers

- A single report claims to show an increased risk for brain and nasal sinus cancers associated with marriage to a smoker. No other researchers have been able to replicate these findings and they must be considered isolated.

Only Hirayama (1984), reporting further on his study of Japanese women, has reported statistically significant associations in women between brain and nasal sinus cancers and spousal smoking.[2]

Breast Cancer

- Some claims have been made for a relationship between husband's smoking and breast cancer in nonsmoking women.

Sandler, et al., (1985) reported a statistically non-significant increased risk for breast cancer in non-smoking women and statistically significant elevated risks for cancers of the endocrine system associated with early life (i.e., childhood) exposure to parental smoking.[7]

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Hirayama (1984), in his discussion of his claim that his data support an elevated risk for all cancers in nonsmoking women whose husbands smoke, suggested that part of the reported increase might be due to breast cancer.[2] In a 1991 article, Wells reports a statistically nonsignificant increased risk of breast cancer using additional data supplied by Hirayama.[8]

Bladder Cancer

- Two case-control studies have specifically examined bladder cancer incidence; neither reported an association between bladder cancer and exposure to ETS at home or at work.

The 1986 Kabat, et al., paper reported that cases and controls in this study did not differ significantly in reporting "sidestream smoke exposure" at home, at work or in transportation.[9] Neither did they differ significantly in whether or not their spouse smoked. The authors concluded that "exposure to sidestream smoke" is not an important factor in bladder cancer in nonsmokers.

The second study to report on bladder cancer is by Burch et al. (1989).[10] It was conducted in Alberta and Ontario, Canada. None of the reported relative risks was statistically significant. The authors concluded that there was no evidence for an effect of

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"passive smoking" on bladder cancer incidence in smokers or nonsmokers.

Cervical Cancer

- Two studies have reported on ETS exposure and the incidence of cervical cancer. Both fail to account sufficiently for confounding factors.

Statistically significant elevated risks for cervical cancer were reported in a 1985 study by Sandler, et al., of patients in North Carolina.[11] This study has been criticized because it did not control for known risk factors such as sexual activity, which is strongly correlated with incidence of cervical cancer.

Slattery, et al., (1989), in a study of women in Utah, reported a statistically significant increased risk of cervical cancer in non-smokers who reported three or more hours of ETS exposure per day (risk estimate of 3.43, 95% CI 1.23-9.54).[12] Although the researchers adjusted for age, church attendance, education and number of sexual partners, these variables do not account for all factors that may contribute to disease.

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Zang, Wynder and Harris authored a letter in response to the Slattery, et al., study.[13] They wrote:

> [T]here clearly is undermatching of control patients with regard to important risk factors including sexual activity, religious background, and education. . . . Since the previously mentioned risk factors are correlated highly with one another as well as with active and passive smoking, the risk estimates relating smoking and cervical cancer may be subject to substantial bias and confounding. . . . In fact, the adjusted odds ratios are probably no more than the leftover effect of variables controlled imperfectly by logistic regression.

In a response, Slattery acknowledged that her group's conclusions "should be verified in other studies."[14]

Childhood Cancers

- Two papers have claimed that their data show that childhood exposure to ETS is related to increased incidence of certain childhood cancers.

Grufferman, et al., (1982) reported a statistically significant relative risk of 3.9 (95% CI 1.5-9.6) for father's cigarette smoking for childhood rhabdomyosarcoma in a case-control study in North Carolina.[15] Only 33 cases were included in the study; only 23 cases were included in the analysis of father's smoking. Conversely, for the 8 cases with maternal smoking, the reported relative risk was 0.8 (95% CI 0.3-2.0). An extremely

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large number of analyses was conducted in this study, suggesting the possibility of data-dredging.

A recent study (John, et al., 1991) reported associations for father's smoking during pregnancy (i.e., a surrogate for ETS exposure of the pregnant woman) in the absence of maternal smoking, with several indices of childhood cancer: all cancers combined (OR = 1.2, 95% CI 0.8-2.1), acute lymphocytic leukemia (OR = 1.4, 95% CI 0.6-3.1), lymphomas (OR = 1.6, 95% CI 0.5-5.4) and brain cancer (OR = 1.6, 95% CI 0.7-3.5).[16] Not one of the associations was statistically significant.

Conclusion

- The studies concerning ETS exposure and cancer other than of the lung are few in number and subject to the same criticisms applicable to the lung cancer studies, e.g., "data-dredging," no assessment of exposure, inadequate control for confounding factors. Additionally, there are only one or two reports on a given cancer endpoint. Without replication of the results, it is not possible to reach any conclusion about ETS exposure and non-pulmonary cancer incidence.

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